06-01-06

AF

OIPE

MAY 30 2006

PATENT & TRADEMARK OFFICE

Please type a plus sign (+) inside this box ☐ +

PTO/SB/21 (6-99)
Approved for use through 09/30/2000. OMB 0651-0031
Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Application Number	09/902,634
Filing Date	JULY 10, 2001
First Named Inventor	AVI ASHKENAZI
Group/Art Unit	1649
Examiner Name	CHERNYSHEV, OLGA N.
Total Number of Pages in This Submission: 21	Attorney Docket Number: 39780-1618 P2C30

ENCLOSURES ***(check all that apply)***

- ☐ Fee Transmittal Form
  - ☐ Fee Attached
- ☐ Amendment / Response
  - ☐ After Final
  - ☐ Version With Markings Showing Changes
  - ☐ Affidavits/declaration(s)
- ☐ Extension of Time Request
- ☐ Information Disclosure Statement
- ☐ Certified Copy of Priority Document(s)
- ☐ Response to Missing Parts/ Incomplete Application
  - ☐ Response to Missing Parts under 37 CFR 1.52 or 1.53
- ☐ Copy of Notice
- ☐ Copy of an Assignment
- ☐ Drawing(s)
- ☐ Licensing-related Papers
- ☐ Petition Routing Slip (PTO/SB/69) and Accompanying Petition
- ☐ Petition to Convert to a Provisional Application
- ☐ Power of Attorney, by Assignee to Exclusion of Inventor Under 37 C.F.R. §3.71 With Revocation of Prior Powers
- ☐ Terminal Disclaimer
- ☐ Small Entity Statement
- ☐ Request for Refund
- ☐ After Allowance Communication to Group
- ☐ Appeal Communication to Board of Appeals and Interferences
- ☒ **APPEAL COMMUNICATION TO GROUP** ***(APPEAL NOTICE, BRIEF, REPLY BRIEF)***
- ☐ Proprietary Information
- ☐ Status Letter
- ☒ **ADDITIONAL ENCLOSURE(S)** ***(PLEASE IDENTIFY BELOW):***
- ☒ **POSTCARD**

Remarks

AUTHORIZATION TO CHARGE DEPOSIT ACCOUNT 08-1641 FOR ANY FEES DUE IN CONNECTION WITH THIS PAPER, REFERENCING ATTORNEY'S DOCKET NO. 39780-1618 P2C30.

SIGNATURE OF APPLICANT, ATTORNEY OR AGENT

Firm *or* Individual name	HELLER EHRMAN LLP	GINGER R. DREGER (Reg. No. 33,055)	
	275 Middlefield Road, Menlo Park, California 94025	Telephone: (650) 324-7000	Facsimile: (650) 324-0638
Signature			
Date	MAY 30, 2006	Customer Number:	35489

CERTIFICATE OF EXPRESS MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 C.F.R. §1.10 on the date indicated below and addressed to: **MAIL STOP APPEAL BRIEF - PATENTS,** Commissioner for Patents, PO Box 1450, Alexandria, Virginia 22313-1450, on this date: **MAY 30, 2006**

Express Mail Label **EL 992 478 111 US**

Typed or printed name	C. FONG		
Signature	C. Fong	Date	MAY 30, 2006

Burden Hour Statement: This form is estimated to take 0.2 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Mail Stop ___, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	)	Examiner: Chernyshev, Olga N.
Avi ASHKENAZI, et al.	)	Art Unit: 1649
Application Serial No. 09/902,634	)	Confirmation No. 1375
Filed: July 10, 2001	)	Attorney's Docket No. 39780-1618 P2C30
For: **SECRETED AND TRANSMEMBRANE POLYPEPTIDES AND NUCLEIC ACIDS ENCODING THE SAME**	)	**Customer No. 35489**

EXPRESS MAIL LABEL NO. EL 992 478 111 US
DATE MAILED: MAY 30, 2006

ON APPEAL TO THE BOARD OF PATENT APPEALS AND INTERFERENCES
APPELLANTS' BRIEF

MAIL STOP APPEAL BRIEF - PATENTS
Commissioner For Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Dear Sir:

On August 29, 2005, the Examiner made a Final rejection of pending Claims 39-43. A Notice of Appeal was filed on November 29, 2005 and an Appeal Brief was filed on March 1, 2006.

A Notification of Non-Compliant Appeal Brief was mailed March 29, 2006, which stated that the Appeal Brief did not fit with the criteria of 37 C.F.R. §41.37(c)(1)(vii)). The following amended Appeal Brief has been corrected to put items under proper headings, as requested by the Examiner. The Board is requested to refer to the Evidence Appendix list submitted with the Appeal Brief dated March 1, 2006 and is not resubmitted herewith.

The following constitutes the amended version of Appellants' Brief on Appeal.

1. REAL PARTY IN INTEREST

The real party in interest is Genentech, Inc., South San Francisco, California, by an assignment of the patent application U.S. Patent Application Serial No. 09/665,350 recorded July 9, 2001, at Reel 011964 and Frame 0181. The present application is a continuation of U.S. Patent Application Serial No. 09/665,350.

2. RELATED APPEALS AND INTERFERENCES

The claims pending in the current application are directed to nucleic acids encoding polypeptides referred to herein as "PRO266." There exist two related patent applications: U.S. Patent Application Serial No. 09/907,824, filed July 17, 2001 (containing claims directed to PRO266 nucleic acids) and U.S. Patent Application Serial No. 09/904,956, filed July 14, 2001 (containing claims directed to PRO266 polypeptides). These applications are also under final rejection from the same Examiner and on similar grounds; appeals of these final rejections are being pursued independently and subsequently herewith.

3. STATUS OF CLAIMS

Claims 39-43 are in this application.

Claims 1-38 and 44 are canceled.

Claims 39-43 stand rejected and Appellants appeal the rejection of these claims.

A copy of the rejected claims involved in the present Appeal is provided as the Claims Appendix.

4. STATUS OF AMENDMENTS

There were no amendments submitted after final rejection. All previous amendments have been entered.

5. SUMMARY OF CLAIMED SUBJECT MATTER

The invention claimed in the present application is related to antibodies, or fragments thereof, that specifically bind to the polypeptide of SEQ ID NO: 91 (termed "PRO266 polypeptides"). The claimed antibodies may be monoclonal antibodies, humanized antibodies, and may be labeled antibodies.

The PRO266 polypeptides were disclosed in the present application and were shown to induce inflammation in the Skin Vascular Permeability assay (SVP assay number 64) (page 210, lines 22-38). The specification also discloses that the polypeptides are related to SLIT proteins and have homology to proteins of the leucine rich repeat superfamily (page 12, lines 24-28).

The PRO266 polypeptides having the amino acid sequence of the polypeptide of SEQ ID NO: 91 are described in the specification, for example, at page 11, line 33 to page 12, line 28; page 39, lines 27-37; page 102, line 32 to page 103, line 3 and in Figure 34, described on page 60, lines 11-12. The nucleic acids encoding PRO266 polypeptides having the amino acid sequence of the polypeptide of SEQ ID NO: 91 are described in the specification at page 39, lines 30-34, for example, and in Figure 33, described on page 60, lines 13-17. The isolation of cDNA nucleic acids encoding PRO266 polypeptides is described in the specification at, for example, Example 14, page 159. Antibodies, production of antibodies and antibody fragments that bind to SEQ ID NO: 91 is described in the specification, for example, at page 73, lines 28-33, page 76, last line to page 77, at pages 199-200, at pages 139-146 and elsewhere in the specification as filed. For instance, support for the preparation and uses of antibodies is found throughout the specification, including, for example, Example 57-59, pages 199-200. Isolated antibodies are defined in the specification at page 139, line 16 onwards. Support for monoclonal antibodies is found in the specification at, for example, page 139, line 32, to page 141, line 13. Support for humanized antibodies is found in the specification at, for example, page 141, line 15, to page 142, line 16. Support for antibody fragments is found in the specification at, for example, page 143, line 8 onwards. Support for labeled antibodies is found in the specification at, for example, pages 144-145, line 16 onwards and page 146, line 33 to page 147, line 6.

Recombinant expression, characteristics and effects of the PRO266 polypeptides were disclosed in the specification, including in Examples 14, 54, 56, 74, and 77. Example 77 (Assay 64) shows that PRO266 polypeptides tested positive in the Skin Vascular Permeability (SVP) assay, an animal model of inflammation, demonstrating that PRO266 polypeptides are effective to induce inflammation. PRO266 polypeptides for which antibodies could be raised,

would therefore have utility in the treatment of conditions of inflammation or characterized by susceptibility to inflammation.

6. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

I. Whether Claims 39-43 are directed to subject matter supported by a specific, substantial and credible utility and so satisfy the utility requirement under 35 U.S.C. §101.

II. Since Claims 39-43 are not directed to subject matter supported by a specific, substantial and credible utility, one skilled in the art would not know how to make and use the invention such that it satisfies the utility requirement under 35 U.S.C. §112, first paragraph.

7. ARGUMENT

Summary of the Arguments:

Issue I: Utility Under 35 U.S.C. §§101/112, First Paragraph

Patentable utility requires an assertion of specific, substantial and credible utility in the application for patent, or a well-recognized utility.

The evidentiary standard to be used in setting forth a rejection is a preponderance of the totality of the evidence under consideration. Thus, to overcome the presumption of truth that an assertion of utility by the Applicant enjoys, the Examiner must establish that it is more likely than not that one of ordinary skill in the art would doubt the truth of the statement of utility. Only after the Examiner has made a proper *prima facie* showing of lack of utility, does the burden of rebuttal shift to the Applicant.

Appellants' asserted patentable utility for the claimed antibodies to PRO266 polypeptides is based upon the data derived from the Skin Vascular Permeability (SVP) assay (Assay 64, Example 77, page 210, lines 22-38). The instant specification discloses, and the Examiner has acknowledged that the SVP assay is a well-established and accepted assay in the art for evaluating test compounds for their ability to induce inflammation (see Final Office Action dated August 29, 2005, Page 3, lines 12-14). For example, the SVP assay has been used in the identification of Vascular Endothelial Growth Factor (VEGF) first known as Vascular Permeability Factor (VPF).

In addition, Appellants have also submitted in their response dated October 4, 2004, a Declaration by Dr. Sherman Fong. Dr. Fong's Declaration clearly establishes the important role that proinflammatory molecules play in treating disease conditions and provides clear examples of clinical applications for inflammatory agents in general, for instance, in treating infections by stimulating immune cells and inducing migration of further immune cells, or in treating autoimmune diseases due to their ability to downmodulate immune responses. Thus, inhibitors of proinflammatory molecules (such as the instantly claimed antibodies) are useful in the treatment of conditions where inflammation may lead to tissue destruction, like in autoimmune diseases, for instance.

In fact, references cited by the Examiner in the Office Action mailed on January 3, 2005, namely, Opdenakker *et al.* and Falcone *et al.* support the Appellants' position that there was vast knowledge available as a whole in the filed of inflammatory diseases at and around the effective date of filing of the instant application (September 17, 1998), which sufficiently provide a nexus between vascular permeability, proinflammation and treatment of a variety of inflammatory disease conditions. Therefore, Appellants submit that, in view of the disclosure of the specification, the art and the expert declaration submitted during prosecution, and despite the Examiner's opinion, one of ordinary skill in the art would have recognized and believed it to be more likely than not that the PRO266 polypeptides and its antibodies are useful, for example, for providing antibodies that inhibit inflammation.

Appellants have thus asserted a specific, substantial and credible utility for the polypeptides disclosed and claimed in the specification, while the Patent Office has failed to meet its initial burden of proof that Appellants' asserted utility is not specific, substantial, or credible, and so has failed to present a *prima facie* case of lack of utility under 35 U.S.C. §§101/112, first paragraph, or to rebut Appellants' arguments and the submitted supportive evidence of record.

Issue II: Enablement Under 35 U.S.C. §112, First Paragraph

Claims 39-43 stand rejected under 35 U.S.C. §112, first paragraph, the Examiner alleging that, since the specification allegedly does not provide a specific, substantial and credible utility,

or a well established utility, one skilled in the art would not know how to use the claimed invention.

However, as discussed previously, the specification indeed does provide a specific, substantial and credible asserted utility for the claimed polypeptides and its antibodies. In addition, the present application includes guidance sufficient to enable one skilled in the art to practice the invention. For example, the specification provides ample guidance to allow the skilled artisan to use the claimed polypeptides for preparing antibodies for inhibiting inflammation when indicated. Such guidance also includes, for example, a detailed protocol for the SVP assay, suitable for measuring inflammation useful for the practice of the invention.

Appellants submit that the present application discloses the utility of the subject matter of the instant claims and that one of skill in the art would know exactly how to use the claimed polypeptides and its antibodies, for instance, for inducing inflammation and for preparing antibodies to reduce inflammation, without any undue experimentation. Accordingly, in view of the disclosure of the present application, one of ordinary skill in the art would understand how to make and use the claimed polypeptides and its antibodies without undue experimentation.

Detailed Arguments:

ISSUE I: Utility Under 35 U.S.C. §§101/112, First Paragraph

Appellants submit that the results of the Skin Vascular Permeability (SVP) assay in the instant specification provides at least one credible, substantial and specific asserted utility for the claimed antibodies to the PRO266 polypeptide as required under 35 U.S.C. §§101/112, first paragraph.

A. The Legal Standard for Utility

According to 35 U.S.C. §101:

> Whoever invents or discovers any new and *useful* process, machine, manufacture, or composition of matter, or any new and *useful* improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title. (Emphasis added).

According to the Utility Examination Guidelines ("Utility Guidelines"), 66 Fed. Reg. 1092 (2001), an invention complies with the utility requirement of 35 U.S.C. §101, if it has at

least one asserted "specific, substantial, and credible utility" or a "well-established utility." Under the Utility Guidelines, a utility is "specific" when it is particular to the subject matter claimed. For example, it is generally not enough to state that a nucleic acid is useful as a diagnostic without also identifying the conditions that is to be diagnosed.

The requirement of "substantial utility" defines a "real world" use, and derives from the Supreme Court's holding in *Brenner v. Manson*, 383 U.S. 519, 534 (1966) stating that "The basic *quid pro quo* contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility." In explaining the "substantial utility" standard, M.P.E.P. §2107.01 cautions, however, that Office personnel must be careful not to interpret the phrase "immediate benefit to the public" or similar formulations used in certain court decisions to mean that products or services based on the claimed invention must be "currently available" to the public in order to satisfy the utility requirement. "Rather, **any reasonable use that an Applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient**, at least with regard to defining a "substantial" utility." (M.P.E.P. §2107.01, emphasis added.) Indeed, the Guidelines for Examination of Applications for Compliance With the Utility Requirement, set forth in M.P.E.P, 2107 II (B) (1) gives the following instruction to patent examiners: "If the Applicant has asserted that the claimed invention is useful for any particular practical purpose ... and the assertion would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility."

Finally, the Utility Guidelines restate the Patent Office's long established position that any asserted utility has to be "credible." "Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record ... that is probative of the applicant's assertions." (M.P.E.P.§ 2107 II(B)(1)(ii)). Such standard is presumptively satisfied unless the logic underlying the assertion is seriously flawed, or if the facts upon which the assertion is based are inconsistent with the logic underlying the assertion (Revised Interim Utility Guidelines Training Materials, 1999).

The case law has clearly established that Applicant's' statements of utility are usually sufficient, unless such statement of utility is unbelievable on its face.[1] The PTO has the initial burden to prove that Applicant's claims of usefulness are not believable on their face.[2] In general, an Applicant's assertion of utility creates a presumption of utility that will be sufficient to satisfy the utility requirement of 35 U.S.C. §101, "unless there is a reason for one skilled in the art to question the objective truth of the statement of utility or its scope."[3, 4]

The well established case law is clearly reflected in the Utility Examination Guidelines ("Utility Guidelines"),[5] which acknowledge that an invention complies with the utility requirement of 35 U.S.C. §101, if it has at least one asserted "specific, substantial, and credible utility" or a "well-established utility." Under the Utility Guidelines, a utility is "specific" when it is particular to the subject matter claimed. For example, it is generally not enough to state that a nucleic acid is useful as a diagnostic without also identifying the conditions that are to be diagnosed.

In explaining the "substantial utility" standard, M.P.E.P. §2107.01 cautions, however, that Office personnel must be careful not to interpret the phrase "immediate benefit to the public" or similar formulations used in certain court decisions to mean that products or services based on the claimed invention must be "currently available" to the public in order to satisfy the utility requirement. "Rather, any reasonable use that an Applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient, at least with regard to defining a 'substantial' utility.'"[6] Indeed, the Guidelines for Examination of Applications for

---

[1] *In re Gazave*, 379 F.2d 973, 154 U.S.P.Q. (BNA) 92 (C.C.P.A. 1967).

[2] *Ibid.*

[3] *In re Langer*, 503 F.2d 1380,1391, 183 U.S.P.Q. (BNA) 288, 297 (C.C.P.A. 1974).

[4] *See also In re Jolles*, 628 F.2d 1322, 206 USPQ 885 (C.C.P.A. 1980); *In re Irons*, 340 F.2d 974, 144 USPQ 351 (1965); *In re Sichert*, 566 F.2d 1154, 1159, 196 USPQ 209, 212-13 (C.C.P.A. 1977).

[5] 66 Fed. Reg. 1092 (2001).

[6] M.P.E.P. §2107.01.

Compliance With the Utility Requirement,[7] gives the following instruction to patent examiners: "If the Applicant has asserted that the claimed invention is useful for any particular practical purpose . . . and the assertion would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility."

Appellants note that the phrase cited above "useful for any practical purpose" merely requires that an invention be useful, and does not require that it be *better* than other competing subject matter: "The Federal Circuit stated that a finding that "an invention that is an 'improvement' is not a prerequisite to patentability" since it "is possible for an invention to be less effective than existing devices but nevertheless meet the statutory criteria for patentability." (*Custom Accessories, Inc. v. Jeffrey-Allan Industries, Inc.)*[8]

In interpreting the utility requirement, in *Brenner v. Manson,*[9] the Supreme Court held that the *quid pro quo* contemplated by the U.S. Constitution between the public interest and the interest of the inventors required that a patent Applicant disclose a "substantial utility" for his or her invention, *i.e.,* a utility "where specific benefit exists in currently available form."[10] The Court concluded that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion. A patent system must be related to the world of commerce rather than the realm of philosophy."[11]

Later, in *Nelson v. Bowler,*[12] the C.C.P.A. acknowledged that tests evidencing pharmacological activity of a compound may establish practical utility, even though they may not establish a specific therapeutic use. The Court held that "since it is crucial to provide researchers

---

[7] M.P.E.P. §2107 II(B)(1).

[8] *Custom Accessories, Inc. v. Jeffrey-Allan Industries, Inc.*, 807 F.2d 955, 1 USPQ2d 1196 (Fed. Cir. 1986).

[9] *Brenner v. Manson,* 383 U.S. 519, 148 U.S.P.Q. (BNA) 689 (1966).

[10] *Id.* at 534, 148 U.S.P.Q. (BNA) at 695.

[11] *Id.* at 536, 148 U.S.P.Q. (BNA) at 696.

[12] *Nelson v. Bowler*, 626 F.2d 853, 206 U.S.P.Q. (BNA) 881 (C.C.P.A. 1980).

with an incentive to disclose pharmaceutical activities in as many compounds as possible, we conclude adequate proof of any such activity constitutes a showing of practical utility."[13]

Moreover, in *Cross v. Iizuka,*[14] the C.A.F.C. reaffirmed *Nelson*, and added that *in vitro* results might be sufficient to support practical utility, explaining that "*in vitro* testing, in general, is relatively less complex, less time consuming, and less expensive than *in vivo* testing. Moreover, *in vitro* results with the particular pharmacological activity are generally predictive of *in vivo* test results, *i.e.,* there is a reasonable correlation there between."[15] The Court perceived, "No insurmountable difficulty" in finding that, under appropriate circumstances, "*in vitro* testing, may establish a practical utility."[16]

Furthermore, M.P.E.P. §2107.03 (III) states that:

> If reasonably correlated to the particular therapeutic or pharmacological utility, data generated using *in vitro* assays, or from testing in an animal model or a combination thereof almost invariably will be sufficient to establish therapeutic or pharmacological utility for a compound, composition or process.

Thus, the legal standard accepts that *in vitro* or animal model data is acceptable utility as long as the data is "reasonably correlated" to the pharmacological utility described.

Compliance with 35 U.S.C. §101 is a question of fact.[17] The evidentiary standard to be used throughout *ex parte* examination in setting forth a rejection is a preponderance of the totality of the evidence under consideration.[18] Accordingly, Appellants submit that in order to overcome the presumption of truth that an assertion of utility by the Applicant enjoys, the Examiner must establish that **it is more likely than not** that one of ordinary skill in the art would

---

[13] *Id.* at 856, 206 U.S.P.Q. (BNA) at 883.

[14] *Cross v. Iizuka*, 753 F.2d 1047, 224 U.S.P.Q. (BNA) 739 (Fed. Cir. 1985).

[15] *Id.* at 1050, 224 U.S.P.Q. (BNA) at 747.

[16] *Id.*

[17] *Raytheon v. Roper*, 724 F.2d 951, 956, 220 U.S.P.Q. (BNA) 592, 596 (Fed. Cir. 1983) *cert. denied,* 469 US 835 (1984).

[18] *In re Oetiker*, 977 F.2d 1443, 1445, 24 U.S.P.Q.2d (BNA) 1443, 1444 (Fed. Cir. 1992).

doubt the truth of the statement of utility. With respect to asserted therapeutic utilities based upon *in vitro* data, an Applicant "does not have to prove that a correlation exists between a particular activity and an asserted therapeutic use of a compound as a matter of statistical certainty."[19] The law requires only that one skilled in the art should accept that such a correlation is **more likely than not to exist**. Appellants respectfully submit that when the proper evidentiary standard is applied, a correlation must be acknowledged.

Thus, to overcome the presumption of truth that an assertion of utility by the Applicant enjoys, the Examiner must establish that it is more likely than not that one of ordinary skill in the art would doubt the truth of the statement of utility. Only after the Examiner made a proper *prima facie* showing of lack of utility, does the burden of rebuttal shift to the Applicant. The issue will then be decided on the totality of evidence.

B. There is Specific, Substantial, and Credible Asserted Utility for PRO266 that is Supported by the Data and the Documentary Evidence

As a preliminary matter, Appellants respectfully submit an assertion for utility for the PRO266 polypeptide molecule and its antibodies has been based upon positive results in the SVP assay which is a **functional** assay. The SVP assay is a well-established assay for identifying proinflammatory molecules for evaluating test compounds for their ability to induce and therefore a positive result in this SVP assay provides strong evidence for a function as a proinflammatory molecule. These results were first disclosed in the international application PCT/US98/19437, filed on 17 September, 1998, priority to which is claimed in the instant application. In addition, the Examiner acknowledged in the Final Office action dated August 29, 2005, on Page 3, lines 12-14 that "based on the information presented in the instant specification, as filed, one skilled in the art would reasonably conclude that the disclosed PRO266 polypeptides could represent a novel proinflammatory molecule" (Emphasis added). Appellants assert that the data enclosed therein for PRO266, and the extensive knowledge available in the art at that time of the present filing on proinflammatory molecules like cytokines, for instance, provide sufficient knowledge on the importance of proinflammatory molecules and

---

[19] M.P.E.P. 2107.03.

its antibodies in combating diseases like cancer or autoimmune diseases, and therefore enable one skilled in the art to make and use the present invention for the treatment of diseases where proinflammatory molecules are useful, like cancer or autoimmune diseases.

C. A *prima facie* case of lack of utility has not been established

However, the Examiner asserts that "the instant specification fails to provide any evidence or sound scientific reasoning that would allow a conclusion that this **instant alleged proinflammatory polypeptide of SEQ ID NO: 91** is useful in treating any particular form of cancer, or is capable of destroying tumor cells, or to treat any or **all** of autoimmune diseases" (emphasis added- see Final Office Action dated August 29, 2005 page 3, lines 16-19). The Examiner adds that the utility is not considered a "substantial utility" and contends that " the art clearly recognizes that class of proinflammatory molecules is characterized by broad range of activities.... In order to use PRO266 polypeptides "as therapeutic target to prepare anti-inflammatory agents, a skilled practitioner would have to first perform a substantial amount of further research to establish its practical utility by discovering the biological role of PRO266 with respect to a particular disease or condition" (see page 4 lines 10-16, Final Office Action dated August 29, 2005). Appellants strongly disagree with this rejection.

As a preliminary matter, Appellants submit that the law pertaining to utility does not require that Appellants show that the invention is useful to "destroy tumor cells, or to treat any or **all** of autoimmune diseases." Patentable utility only requires that an assertion of a specific, substantial and credible utility, or a well-recognized utility be made in the application, and Appellants believe they have made a proper case for utility in this instance as discussed above and below. Appellants also believe that the Examiner is applying a heightened standard in this rejection by requiring a showing that "the invention is useful to destroy tumor cells, or to treat any or **all** of autoimmune diseases," which is improper. The law pertaining to "substantial" utility and "currently available form" have been clearly discussed above and are also discussed below.

The fact remains that the results of the SVP assay were positive, indicating induction of inflammation. Thus, the Examiner 's concern that the results were an invitation to experiment further, do not negate the positive results of the assay, that is PRO266 is a proinflammatory

molecule, and further, do not negate the assertion of utility for PRO266 polypeptides. As discussed above, one of ordinary skill in the art in possession of these results would, more likely than not, acknowledge that the PRO266 polypeptides are useful as proinflammatory agents and the Examiner herself had acknowledged this utility in the Final Office Action on Page 3, lines 18-20. Yet, the Examiner sometimes refers to the PRO266 molecule as an "**alleged** proinflammatory polypeptide of SEQ ID NO: 91" in the Final Office action, which is contradictory. Appellants believe that there should be no issue regarding the PRO266 polypeptide as a proinflammatory molecule based on positive the results of the SVP assay.

Moreover, Appellants submit that the results of the SVP assay, which identified a pharmacological activity for PRO266, suffices to provide utility in itself. Regarding utility based on pharmacological results, Appellants submit that the Courts have clearly stated and repeatedly found that the mere identification of a pharmacological activity for a compound that is relevant to an asserted pharmacological use provides an "immediate benefit to the public" and thus satisfies the utility requirement. As the Court of Customs and Patent Appeals held in *Nelson v. Bowler*:

> Knowledge of the pharmacological activity of any compound is obviously beneficial to the public. It is inherently faster and easier to combat illnesses and alleviate symptoms when the medical profession is armed with an arsenal of chemicals having known pharmacological activities. Since it is crucial to provide researchers with an incentive to disclose pharmacological activities in as many compounds as possible, we conclude that adequate proof of any such activity constitutes a showing of practical utility.

Nelson v. Bowler, 626 F.2d 853, 856, 206 USPQ 881, 883 (CCPA 1980); *In re Jolles*, 628 F.2d 1322, 206 USPQ 885 (CCPA 1980); *In re Cross v. Iizuka*, 753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985) (Emphasis added). Similarly, courts have found utility for therapeutic inventions despite the fact that an applicant is at a very early stage in the development of a pharmaceutical product or therapeutic regimen based on a claimed pharmacological or bioactive compound or composition. For instance, in *Cross v. Iizuka*, 753 F.2d 1040, 1051, 224 USPQ 739, 747-48 (Fed. Cir. 1985), the Federal Circuit, commented on the significance of data from *in vitro* testing that showed pharmacological activity as follows:

> We perceive no insurmountable difficulty, under appropriate circumstances, in finding that the first link in the screening chain, in vitro testing, may establish a practical utility for the compound in question. Successful in vitro testing will

> marshal resources and direct the expenditure of effort to further in vivo testing of the most potent compounds, thereby providing an immediate benefit to the public, analogous to the benefit provided by the showing of an in vivo utility.

Cross v. Iizuka, 753 F.2d 1040, 1051, 224 USPQ 739, 747-48 (Fed. Cir. 1985). Therefore, the Federal Circuit has reiterated that therapeutic utility, sufficient under the patent laws is **not to be confused with the requirements of the FDA** with regard to safety and efficacy of drugs to marketed in the United States (also see M.P.E.P. §2107.01). Therefore, Appellants submit that "substantial amount of further research" is **not** required by the skilled practitioner to establish a practical utility or for discovering the biological role of PRO266. Appellants have already asserted a utility and a biological role for PRO266 as a proinflammatory molecule that is useful to treat diseases and conditions as further discussed below.

Appellants point out that the role of proinflammatory molecules in the art is further exemplified by Opdenakker *et al.* and Falcone *et al.*, the two references cited by the Examiner on January 3, 2005, which in fact support the Appellants' position that the knowledge available, as a whole, in the field of inflammatory diseases, at and around the effective date of filing of the instant application (September 17, 1998), was extensive such that one skilled in the art in immunology would clearly recognize a specific and substantial utility for a molecule involved in inflammation. These peer-reviewed references teach that proinflammatory molecules like PRO266 do have a broad range of roles and that itself points to specific uses for PRO266. These exemplary references clearly showed that proinflammatory molecules play a primary role in the pathology of many diseases and also provide a nexus between proinflammation and the treatment of a variety of inflammatory disease conditions like tumorigenesis, generalized inflammation, diabetic retinopathy, autoimmune conditions, etc. Therefore, one skilled in the art would easily see that, (1) PRO266 is useful for inducing inflammation, and so PRO266's proinflammatory properties are useful to stimulate immune cells already present and/or to induce recruitment of other inflammatory cells into a particular site, which can be useful to combat infection or a site with a solid tumor, and this is a useful property to combat infection or tumor progression, for instance, and was discussed extensively in the supportive references cited in the Fong Declaration and also in the Opdenakker *et al.* reference; and (2) PRO266's anti-inflammatory properties may be useful in the downmodulation of inflammatory responses useful in controlling

autoimmune responses and preventing the destructive effects of inflammation therein. Thus, PRO266 is also useful for preparing anti-inflammatory antibodies (useful, for example, to treat undesirable inflammatory conditions). Both these uses are substantial, specific and credible utilities based on the discussions above, the discussions in the Fong Declaration and the extensive knowledge in the art.

In view of the above, Appellants submit that a valid case for utility has been made and would be considered credible by a person of ordinary skill in the art. Indeed, the logic underlying Appellants' assertion that the PRO266 polypeptides would be useful in inducing inflammation or in providing antibodies for inhibiting inflammation is not inconsistent with the general knowledge in the art, and would be considered credible by a person skilled in the art. Accordingly, Appellants respectfully submit that the Examiner's comments fail to support a *prima facie* case of lack of utility.

In summary, Appellants respectfully submit that the Patent Office has failed to meet its initial burden of proof that Appellants' claims of utility are not substantial or credible. Accordingly, Appellants believe the rejections of Claims 39-43 under 35 U.S.C. §101, to be improper, and respectfully request withdrawal of these rejections.

Issue II: Enablement Under 35 U.S.C. §112, First Paragraph

Appellants refer to the arguments and information presented above under Issue I with respect to utility. These arguments are incorporated by reference herein. Appellants respectfully submit that as described above under Issue I, the data from the SVP assay disclosed in Example 77 provides a specific, substantial and credible utility for the claimed invention and, therefore, the present specification teaches one of ordinary skill in the art "how to use" the claimed invention without undue experimentation, as described above.

The present claims recite polypeptides that induce an inflammatory response. The claimed PRO266 polypeptides are useful for inducing inflammation and for providing antibodies for reducing inflammation as discussed above. As discussed above, support for this recitation is found in Example 77 (page 210, lines 22) which describes a dye-based proinflammatory cell infiltration assay in which PRO266 polypeptides induce inflammation, described as "inducing mononuclear cell, eosinophil and PMN infiltration at the site of injection of the animal"

(page 210, lines 23-24 of the specification). The results of Example 77 provide the skilled artisan with guidance on how to use such a polypeptide and its antibodies.

The specification provides detailed guidance as to how to identify and make polypeptides having varying amino acid sequence identity to PRO266 polypeptides. The specification also provides ample guidance to allow the skilled artisan to identify those polypeptides which meet the limitations of the claims, including a detailed protocol for the SVP assay. Therefore, Appellants respectfully submit that the specification provides ample guidance such that one of skill in the art could readily test a polypeptide to determine whether it is capable of inducing inflammation by the methods set forth in Example 77.

Thus, based on the information disclosed in the specification and the information which was available in the art, one skilled in the art knew how to practice the claimed invention, at the effective priority date of this application, without undue experimentation. As the M.P.E.P. states, "The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. *In re Certain Limited-charge cell Culture Microcarriers, 221 USPQ 1165, 1174* (Int'l Trade Comm'n 1983), *aff'. sub nom., Massachusetts Institute of Technology v A.B. Fortia,* 774 F.2d 1104, 227 USPQ 428 (Fed. Cir. 1985) M.P.E.P. §2164.01. A considerable amount of experimentation is permissible, if it is merely routine. As the M.P.E.P. states, "[t]he fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation."[20]

Appellants thus submit that one of ordinary skill in the art would understand how to make and use the recited polypeptides and its antibodies without undue experimentation. Accordingly, Appellants respectfully submit that rejections of Claims 39-43 under 35 U.S.C. §112, first paragraph, are overcome.

CONCLUSION

For the reasons given above, Appellants submit that the Skin Vascular Permeability assay disclosed in Example 77 of the specification provides at least one asserted specific and

---

[20] M.P.E.P. §2164.01 citing *In re Certain Limited-charge Cell Culture Microcarriers,* 221 USPQ 1165, 1174 (Int'l Trade Comm'n 1983), *aff' sub nom. Massachusetts Institute of Technology v A.B. Fortia*, 774 F.2d 1104, 227 USPQ 428 (Fed. Cir. 1985).

substantial patentable utility for the claimed antibodies to PRO266 in Claims 39-43, and that one of ordinary skill in the art would accept this asserted utility as credible and would understand how to make and use the claimed antibodies to PRO266. Therefore, Claims 39-43 meet the requirements of 35 USC §101 and 35 USC §112, first paragraph. Accordingly, reversal of all the rejections of Claims 39-43 is respectfully requested.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. **08-1641** (referencing Attorney's Docket No. **39780-1618 P2C30**.

Respectfully submitted,

Date: May 30, 2006

By: _____
Ginger R. Dreger (Reg. No. 33,055)

HELLER EHRMAN LLP
275 Middlefield Road
Menlo Park, California 94025-3506
Telephone: (650) 324-7000
Facsimile: (650) 324-0638

8. CLAIMS APPENDIX

Claims on Appeal

39. An isolated antibody that specifically binds to the polypeptide of SEQ ID NO:91.

40. The antibody of Claim 39 which is a monoclonal antibody.

41. The antibody of Claim 39 which is a humanized antibody.

42. The antibody of Claim 39 which is an antibody fragment.

43. The antibody of Claim 39 which is labeled.

9. EVIDENCE APPENDIX (PREVIOUSLY SUBMITTED)

1. Declaration of Sherman Fong, Ph.D. under 35 C.F.R 1.132, with attached Exhibits A-I:

Exhibit A: Miles *et al.*, J. Physiol. **118**:228-257 (1952).

Exhibit B: Regulation of Leukocyte Movement.

Exhibit C: Baggiolini *et al.*, *Annu. Rev. Immunol.* **15**:675-705 (1997).

Exhibit D: Streiter, *et al. J. Biol. Chem.* **270(45)**:27348-27357 (1995).

Exhibit E: Udaka *et al.*, *Proc. Soc. Exp. Biol. Med.* **133**:1384-1387 (1970).

Exhibit F: Hirahara, *et al.*, *Thrombosis Res.* **71**:139-148 (1993).

Exhibit G: Senger *et al.*, *Science* **219**:983-985 (1983), and Elicieri *et al.*, *Molecular Cell* **4**:915-924 (1999).

Exhibit H: Yeo *et al.*, *Clin. Chem.* **38(1)**:71-75 (1992).

Exhibit I: Image of guinea pig skin showing a positive reaction to a PRO polypeptide.

2. Opdenakker *et al.*, *Verh. K. Acad. Geneeskd. Belg.*, **64**: 105-36 (2002).

3. Falcone *et al.*, *Curr. Opin. Immunol.*, **11**: 670-6 (1999).

Item 1 was submitted with Appellants' Response filed October 4, 2004, and noted as considered by the Examiner in the Office Action mailed January 3, 2005.

Items 2-3 were made of record by the Examiner in the Office Action mailed January 3, 2005.

10. RELATED PROCEEDINGS APPENDIX

None - no decision rendered by a Court or the Board in any related proceedings identified above.

SV 2210404 v1
5/30/06 9:31 AM (39780.1618)